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Scientists Produce Mouse Eggs from Embryonic Stem Cells

by Steven Bradt

Researchers at the School have created the first mammalian gametes grown in vitro directly from embryonic stem cells. The work, in which mouse stem cells placed in Petri dishes—without any special growth or transcription factors—grew into oocytes and then into embryos, was reported in early May on the website of the journal *Science*.

The results demonstrate that even outside the body embryonic stem cells remain totipotent, or capable of generating any of the body's tissues, said lead researcher **Dr. Hans R. Schöler**, professor of reproduction medicine and director of Penn's Center for Animal Transgenesis and Germ Cell Research.

"Most scientists have thought it impossible to grow gametes from stem cells outside the body, since earlier efforts have yielded only somatic cells," said Schöler. "We found that not only can mouse embryonic stem cells produce oocytes, but that these oocytes can then enter meiosis, recruit adjacent cells to form structures similar to the follicles that surround and nurture natural mouse eggs, and develop into embryos."

Schöler said oocyte development in vitro may offer a new way for embryonic stem cells to be produced artificially, sidestepping the ethical concerns articulated by President Bush and others. Implanting a regular nucleus from any of the body's cells into such an oocyte would yield a totipotent stem cell.

The findings may force legal revisions in nations such as Germany whose lawmakers, assuming that stem cells' potency outside the body was limited, have passed legislation banning research with totipotent stem cells.

The Penn scientists pulled off this feat using a gene called Oct4 as a genetic marker. After the stem cells were plated in a regular Petri dish—densely but without special feeder cells or growth factors—the scientists used fluorescent markers linked to Oct4 and other telltale genes to assay oocyte development. After 12 days in culture, the cells organized into colonies of variable size. Shortly thereafter, individual cells detached from these colonies.

"These germ cells then accumulated a coating of cells similar to the follicles surrounding mammalian eggs," Schöler said. "Starting on day 26, oocyte-like cells were released into the

culture—similar to ovulation—and by day 43, embryo-like structures arose through parthenogenesis, or spontaneous reproduction without sperm."

In the experiment described in *Science*, both male- and female-derived stem cells developed into female gametes. Schöler and colleagues now plan to test whether oocytes developed in vitro can be fertilized.

"We would like to use these oocytes as a basis for therapeutic cloning, and hope that our results can be replicated with human embryonic stem cells," Schöler said.

Schöler was joined in the research by **Karin Hübner, James Kehler, Rolland Reinbold, Rabindranath de la Fuente, and Michele Boiani** of Penn's School of Veterinary Medicine; Lane K. Christenson, Jennifer Wood, and Jerome Strauss III from Penn's School of Medicine; and Guy Fuhrmann of the Centre de Neurochimie in France. The work was funded by the National Institutes of Health, the Marion Dilley and David George Jones Funds, the Commonwealth and General Assembly of Pennsylvania, and the Association pour la Recherche sur la Cancer.

Penn President Judith Rodin to Step Down in June 2004

Judith Rodin, CW'66, president of the University of Pennsylvania since 1994, announced on June 20, 2003, that she intends to step down



from the office when she completes her 10-year term in June 2004. Rodin became Penn's president on July 1, 1994, coming to Penn from Yale, where she had been Provost. She was

the first woman to be named to the presidency of an Ivy League institution, and the first Penn alumna to serve as president.

During nearly a decade of service, Rodin has guided the University through a period of unprecedented growth and development that has transformed Penn's academic core and dramatically enhanced the quality of life on campus and in the surrounding community. Under her leadership, Penn has invigorated its

resources, doubling its research funding and tripling both its annual fundraising and the size of its endowment; created Penn Medicine; launched a comprehensive and widely acclaimed neighborhood revitalization program; attracted record numbers of undergraduate applicants, creating Penn's most selective classes ever; risen in the *U.S. News & World Report* rankings of top national research universities from 16th in 1994 to 4th in 2002; established new interdisciplinary institutes and created over a dozen groundbreaking interdisciplinary, multi-school, undergraduate, and graduate degree programs throughout the University; planned or completed new buildings and major renovations in every school and center; and expanded its international programs and collaborations. Faculty excellence has risen dramatically and there has been significant investment in leading-edge graduate and professional degree programs.

"Serving Penn these past years has been an extraordinary privilege and an exhilarating experience," Rodin said. "This is a remarkable

community of amazing depth and breadth, and I am grateful to the Trustees for their support and for giving me the opportunity to work with so many talented and creative individuals. I am very proud of all that our faculty, staff, students, alumni and community partners have together enabled Penn to accomplish.

"The decision to step down has been an extremely difficult one for me to make, but I believe it is the right time for Penn. We have successfully fulfilled our first strategic plan and with the next plan conceived and ready to launch, it is time for the next era of leadership. I love this institution and will always remain a part of it."

The executive committee of Penn's Board of Trustees will appoint in the months ahead a presidential search committee, to be comprised of trustees, faculty, and students, which will be chaired by James S. Riepe, W'65 WG'67, the Board chairman. For more information, visit the "Judith Rodin: An Enduring Legacy" website at <www.upenn.edu/pennnews/rodin_legacy/>.